labeled probe molecules by quenching a first florescence provided by the labeled probe molecules.

16. (Twice Amended) A method for assessing the presence of a target molecule in a cell or tissue sample comprising the steps of:

a. providing a microarray having a surface area comprising attached labeled probe molecules in quadrants, said labeled probe molecules including at least one nucleotide analog capable of fluorescence;

b. detecting fluorescence from said at least one nucleotide analog capable of fluorescence expressed within quadrants a first time;

c. applying a sample comprising unlabeled target sequences to the microarray;

d. providing a sufficient condition and time for target molecules to selectively pair with complementary labeled probe molecules;

e. detecting fluorescence from said at least one nucleotide analog capable of fluorescence expressed within quadrants a second time;

f. comparing the fluorescence expressed between the first time and the second time for each quadrant;

g. repeating steps c - f until levels of fluorescence decrease towards a level approaching zero and/or about background levels; and

h. the difference between fluorescence in that of step f and that of step c providing target/probe pair quantification.

17. (Twice Amended) A method for quantifying the amount of a target molecule in solution comprising the steps of:

a. ing a first substrate having a surface area comprising a known number of cules, said labeled probe molecules include at least one nucleotide analog labeled p ence;

capable tecting a first level of nucleotide analog fluorescence expressed by the labeled s on the first substrate;

contacting the first substrate with a volume of sample containing unlabeled target equences;

providing a sufficient condition and time for unlabeled target molecules to ly pair with the labeled probe molecules;

e. removing the first substrate and detecting the level of nucleotide analog fluorescence expressed by said known number of labeled probe molecules after exposure to the sample containing unlabeled target molecules;

f. where the level of nucleotide analog fluorescence expression of the first substrate is substantially reduced to levels substantially similar to background levels, repeating steps a. through e. with subsequent substrates, having surface areas comprising known numbers of labeled probe molecules; and

g. calculating the amount of target molecule in the volume of sample by adding the known number of labeled probe molecules present on the first substrate and subsequent substrates contacted with the sample, wherein the levels of nucleotide analog fluorescence expression of the substrates are reduced to a level approaching zero relative to the levels prior to contacting the sample, whereby said amount of target molecule is quantified.

18. (Amended) The method of claim 17, wherein the level of label expression is evaluated using a flow cytometer.

20. (Twice Amended) A method for monitoring the hybridization of target and probe by complementation, comprising:

a. incorporating fluorescent nucleotide analogs into probes;

b. detecting a first level of fluorescence emanating from probes of step a;

d. hybridizing a target with said probes thereby forming a probe-target complex;

e. detecting a second level of fluorescence emanating from said probe-target complex after hybridization of probe and target;

f. comparing the first and second levels of fluorescence between that of step b and that of step e, and wherein said difference between second and first levels is less than said first level of step b;

g. washing of unhybridized target;

h. repeating steps d - g until the difference between the first and second levels of fluorescence approaches approximately zero and/or about background levels; and

i. quantifying the amount of target based upon said target's hybridization and subsequent quenching of said first level of fluorescence toward a level approaching zero.

22. (Thrice Amended) A method for monitoring the hybridization of a probe and a target comprising, providing a fluorescently labeled probe, said fluorescence being provided by a nucleotide analog capable of fluorescence and is incorporated, thereby providing a detectable first level of fluorescence and providing a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is lower than the first level and approaches zero, said decrease in fluorescence quantifying the amount of complementary unlabeled target.

23. (Thrice Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe, said fluorescently labeled probe being fluorescent due to the incorporation of at least one nucleotide analog thereby providing a detectable first level of fluorescence, and providing a detectable second level of fluorescence

when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is significantly lower than the first level and said second levels of fluorescence approach zero and/or about background levels.

25. (Thrice Amended) A method for monitoring the hybridization of a probe and a target comprising supplying a fluorescently labeled probe, said fluorescently labeled probe being fluorescent due to the incorporation of at least one nucleotide analog capable of fluorescence, thereby providing a detectable first level of fluorescence, and a detectable second level of fluorescence when the labeled probe is hybridized to a complementary unlabeled target, wherein the second level is approximately zero and the first level is greater than zero, and utilizing said reduction of fluorescence to approximately zero for quantifying said complementary unlabeled target.

29. (Thrice Amended) A substrate having a known and quantified plurality of probes, wherein said probes are fluorescently labeled by incorporation of at least one nucleotide analog, the labeled probe providing a detectable first level of fluorescence, and when hybridized to a complementary target having no nucleotide analogs incorporated therein, providing a second level of fluorescence, wherein the second level approaches zero, and wherein said known and quantified plurality of probes provides for quantification of said complementary target.

31. (Twice Amended) A substrate having a surface area, the surface area comprising attached and quantified labeled probe molecules, said probe further comprising a fluorescent label, said fluorescent label including at least one nucleotide analog incorporated as part of a nucleotide sequence defining said labeled probe molecules.

34. (Amended) The method of claim 31 whereby the labeled probe molecules are nucleotide analogs including 2-amino purine for adenosine or guanine; ribonucleoside or 2,6-diamino ribonucleoside, formycin A, formycin B, oxyformycin B, toyocamycin, sangivamycin, pseudoouridine, showdomycin, minimycin, pyrazomycin, 5-amino-formycin A, 5-amino-formycin B or 5-oxo-formycin A for adenosine; 4-amino-pyrazolo [3,4d] pyrimidine, 4,6-diamino-pyrazolo [3,4d] pyrimidine, 4-amino-6-oxo-pyrazolo [3,4d] pyrimidine, 4-oxo-pyrazolo

[3,4d] pyrimidine, 4-oxo-6-amino-pyrazolo [3,4d] pyrimidine, 4,6-dioxo-pyrazolo [3,4d] pyrimidine, pyrazolo [3,4d] pyrimidine, 6-amino-pyrazolo [3,4d] pyrimidine or 6-oxo-pyrazolo [3, 4d] pyrimidine for cytosine or thymidine

35. (Amended) The substrate of claim 31 whereby the incorporated nucleotide analog is 2-aminopurine replacing adenosine or guanine nucleotides.

39. (Amended) The substrate of claim 1 whereby the incorporated nucleotide analog is 2-aminopurine replacing at least one endemic adenosine or guanine nucleotide.

REMARKS

Applicant has carefully considered the Office Action of September 17, 2002 and sets forth detailed responses herein. Applicant has amended specific claims addressed by the Examiner in the Office Action dated September 17, 2002 and during the informative interviews kindly granted by the Examiner on December 10 and 11, 2002. Claims marked up to show changes made in this amendment are provided as addendum pages.

Applicant's agent wishes to thank the Examiner for her informative and helpful discussions regarding the instant application and, in particular, the discussions relating to the teachings of references previously cited.

Claims 1, 16, 17, 18, 20, 22, 23, 25, 29, 31, 34, 35 and 39 have been amended to more particularly point out and distinctly claim certain aspects of Applicant's invention, in light of said discussions. Support for such amendments may be found on pages 2-3 and 8-9 of the specification. The amended claims do not introduce new subject matter. Claims 19, 22, 24, 26, 27 and 30 have been cancelled without prejudice in order to streamline prosecution of the present case.

Reconsideration and allowance of all of pending claims in view of the above amendments and the following remarks is respectfully requested.